

# WHAT IS CLAIMED IS:

1. A method of inducing apoptosis in a human cancer cell, the method comprising: introducing into the cell a ribozyme that inhibits metallothionein expression, wherein the ribozyme comprises a nucleotide sequence selected from the group consisting of:

5'-GCACUUCUCUCUGAUGAGUCCGUGAGGACGAAAUGCCCCUUUGC-3'

(SEQ ID NO:1) (Hu MT-Ia Rz);

5'-CCCCUUUGCACUGAUGAGUCCGUGAGGACGAAACGCAGCCCCU-3'

(SEQ ID NO:2) (Hu MT-Ie/r Rz);

5'-GCACUUCUCUCUGAUGAGUCCGUGAGGACGAAACGCCCCUUUGC-3'

(SEQ ID NO:3) (Hu MT-If Rz);

5'-GAGCCUUUGCACUGAUGAGUCCGUGAGGACGAAACACAGCCCCU-3'

(SEQ ID NO:4) (Hu MT-Ib Rz);

5'-CCCCUUUGCACUGAUGAGUCCGUGAGGACGAAAUGCAGCCCCU-3'

(SEQ ID NO:5) (Hu MT-Ighlx/-II Rz);

5'-GCGCCUUUGCACUGAUGAGUCCGUGAGGACGAAACACAGCCCCU-3'

(SEQ ID NO:6) (Rz1-2); and

5'-CCUCUUUGCACUGAUGAGUCCGUGAGGACGAAAUGCAGCCCCU-3'

(SEQ ID NO:7) (Rz4-9).

2. The method of claim 1, wherein the human cancer cell is a cell *in vitro*.

3. The method of claim 1, wherein the human cancer cell is a cell *in vivo*.

4. The method of claim 3, wherein introducing the ribozyme into the cell comprises injecting the ribozyme directly into a tumor comprising the cell *in vivo*.

5. The method of claim 1, wherein the ribozyme is a hammerhead ribozyme.

6. The method of claim 1, wherein the human cancer cell is a prostate cancer cell, a breast cancer cell, or an ovarian cancer cell.

7. A method of inducing apoptosis in a human cancer cell, the method comprising: introducing into the cell a nucleic acid vector comprising a nucleotide sequence encoding a ribozyme that inhibits metallothionein expression, wherein the ribozyme comprises a nucleotide sequence selected from the group consisting of:

5'-GCACUUCUCUCUGAUGAGUCCGUGAGGACGAAAUGCCCCUUUGC-3'  
(SEQ ID NO:1) (Hu MT-Ia Rz);

5'-CCCCUUUGCACUGAUGAGUCCGUGAGGACGAAACGCAGCCCU-3'  
(SEQ ID NO:2) (Hu MT-Ie/r Rz);

5'-GCACUUCUCUCUGAUGAGUCCGUGAGGACGAAACGCCCUUUGC-3'  
(SEQ ID NO:3) (Hu MT-If Rz);

5'-GAGCCUUUGCACUGAUGAGUCCGUGAGGACGAAACACAGCCCU-3'  
(SEQ ID NO:4) (Hu MT-Ib Rz);

5'-CCCCUUUGCACUGAUGAGUCCGUGAGGACGAAAUGCAGCCCU-3'  
(SEQ ID NO:5) (Hu MT-Ighlx/-II Rz);

5'-GCGCCUUUGCACUGAUGAGUCCGUGAGGACGAAACACAGCCCU-3'  
(SEQ ID NO:6) (Rz1-2); and

5'-CCUCUUUGCACUGAUGAGUCCGUGAGGACGAAAUGCAGCCCU-3'  
(SEQ ID NO:7) (Rz4-9).

8. The method of claim 7, wherein the human cancer cell is a cell *in vitro*.

9. The method of claim 7, wherein the human cancer cell is a cell *in vivo*.

10. The method of claim 7, wherein introducing the vector into the cell comprises injecting the vector directly into an *in vivo* tumor comprising the cell.

11. The method of claim 7, wherein the human cancer cell is a prostate cancer cell, a breast cancer cell, or an ovarian cancer cell.

12. The method of claim 11, wherein the nucleotide sequence is operatively linked to a prostate tissue-specific promoter, a breast-specific promoter, or an ovary-specific promoter.

13. A method of inhibiting growth of a tumor, the method comprising introducing into cells of the tumor a ribozyme that inhibits metallothionein expression, wherein the ribozyme comprises a nucleotide sequence selected from the group consisting of:

5'-GCACUUCUCUCUGAUGAGUCCGUGAGGACGAAAUGCCCCUUUGC-3'  
(SEQ ID NO:1) (Hu MT-Ia Rz);

5'-CCCCUUUGCACUGAUGAGUCCGUGAGGACGAAACGCAGCCCU-3'  
(SEQ ID NO:2) (Hu MT-Ie/r Rz);

5'-GCACUUCUCUCUGAUGAGUCCGUGAGGACGAAACGCCCCUUUGC-3'  
(SEQ ID NO:3) (Hu MT-If Rz);

5'-GAGCCUUUGCACUGAUGAGUCCGUGAGGACGAAACACAGCCCU-3'  
(SEQ ID NO:4) (Hu MT-Ib Rz);

5'-CCCCUUUGCACUGAUGAGUCCGUGAGGACGAAAUGCAGCCCU-3'  
(SEQ ID NO:5) (Hu MT-Ighlx/-II Rz);

5'-GCGCCUUUGCACUGAUGAGUCCGUGAGGACGAAACACAGCCCU-3'  
(SEQ ID NO:6) (Rz1-2); and

5'-CCUCUUUGCACUGAUGAGUCCGUGAGGACGAAAUGCAGCCCU-3'  
(SEQ ID NO:7) (Rz4-9).

14. The method of claim 13, wherein introducing the ribozyme into the cells of the tumor comprises injecting the ribozyme directly into the tumor.

15. The method of claim 13, wherein the tumor is a human prostate tumor, human breast tumor, or human ovarian tumor.

16. A method of inhibiting growth of a tumor, the method comprising introducing into cells of the tumor a nucleic acid vector comprising a nucleotide sequence encoding a ribozyme that inhibits metallothionein expression, wherein the ribozyme comprises a nucleotide sequence selected from the group consisting of:

5'-GCACUUCUCUCUGAUGAGUCCGUGAGGACGAAAUGCCCCUUUGC-3'  
(SEQ ID NO:1) (Hu MT-Ia Rz);

5'-CCCCUUUGCACUGAUGAGUCCGUGAGGACGAAACGCAGCCCU-3'  
 (SEQ ID NO:2) (Hu MT-Ie/r Rz);  
 5'-GCACUUCUCUCUGAUGAGUCCGUGAGGACGAAACGCCCCUUUGC-3'  
 (SEQ ID NO:3) (Hu MT-If Rz);  
 5'-GAGCCUUUGCACUGAUGAGUCCGUGAGGACGAAACACAGCCCU-3'  
 (SEQ ID NO:4) (Hu MT-Ib Rz);  
 5'-CCCCUUUGCACUGAUGAGUCCGUGAGGACGAAAUGCAGCCCU-3'  
 (SEQ ID NO:5) (Hu MT-Ighlx/-II Rz);  
 5'-GCGCCUUUGCACUGAUGAGUCCGUGAGGACGAAACACAGCCCU-3'  
 (SEQ ID NO:6) (Rz1-2); and  
 5'-CCUCUUUGCACUGAUGAGUCCGUGAGGACGAAAUGCAGCCCU-3'  
 (SEQ ID NO:7) (Rz4-9).

17. The method of claim 16, wherein introducing the vector into the cells of the tumor comprises injecting the vector directly into the tumor.

18. The method of claim 16, wherein the tumor is a human prostate tumor, a human breast tumor, or a human ovarian tumor.

19. The method of claim 16, wherein the nucleotide sequence is operatively linked to a prostate tissue-specific promoter, a breast tissue-specific promoter, or an ovarian tissue-specific promoter.

20. A method of enhancing the effectiveness of cancer therapy, the method comprising: introducing into cancer cells of a patient a ribozyme that inhibits metallothionein expression; and administering to the patient a therapeutically effective amount of a cancer therapy agent, wherein the ribozyme comprises a nucleotide sequence selected from the group consisting of:

5'-GCACUUCUCUCUGAUGAGUCCGUGAGGACGAAAUGCCCCUUUGC-3'  
 (SEQ ID NO:1) (Hu MT-Ia Rz);  
 5'-CCCCUUUGCACUGAUGAGUCCGUGAGGACGAAACGCAGCCCU-3'

(SEQ ID NO:2) (Hu MT-Ie/r Rz);

5'-GCACUUCUCUCUGAUGAGUCCGUGAGGACGAAACGCCCCUUUGC-3'

(SEQ ID NO:3) (Hu MT-If Rz);

5'-GAGCCUUUGCACUGAUGAGUCCGUGAGGACGAAACACAGCCCU-3'

(SEQ ID NO:4) (Hu MT-Ib Rz);

5'-CCCCUUUGCACUGAUGAGUCCGUGAGGACGAAAUGCAGCCCU-3'

(SEQ ID NO:5) (Hu MT-Ighlx/-II Rz);

5'-GCGCCUUUGCACUGAUGAGUCCGUGAGGACGAAACACAGCCCU-3'

(SEQ ID NO:6) (Rz1-2); and

5'-CCUCUUUGCACUGAUGAGUCCGUGAGGACGAAAUGCAGCCCU-3'

(SEQ ID NO:7) (Rz4-9).

21. The method of claim 20, wherein introducing the ribozyme into the cells comprises injecting the ribozyme directly into an *in vivo* tumor comprising the cells.

22. The method of claim 20, wherein the tumor is a human prostate tumor, a human breast tumor, or a human ovarian tumor.

23. The method of claim 20, wherein the cancer therapy is chemotherapy.

24. The method of claim 23, wherein the cancer therapy agent is selected from the group consisting of cisplatin, estramustine, vinblastine, etoposide, paclitaxel, taxotere, docetaxel, doxorubicin, ketocanazole, and cyclophosphamide.

25. The method of claim 20, wherein the therapy is radiation therapy

26. The method of claim 25, wherein the type of radiation therapy is selected from the group consisting of external beam radiation therapy, brachytherapy, and <sup>125</sup>I administration.

27. A method of enhancing the effectiveness of cancer therapy, the method comprising: introducing into the cancer cells of a patient a nucleic acid vector comprising a nucleotide sequence encoding a ribozyme that inhibits metallothionein expression; and administering to the patient a therapeutically effective amount of the cancer therapy, wherein the ribozyme comprises a nucleotide sequence selected from the group consisting of:

5'-GCACUUCUCUCUGAUGAGUCCGUGAGGACGAAAUGCCCCUUUGC-3'

(SEQ ID NO:1) (Hu MT-Ia Rz);

5'-CCCCUUUGCACUGAUGAGUCCGUGAGGACGAAACGCAGCCCCU-3'

(SEQ ID NO:2) (Hu MT-Ie/r Rz);

5'-GCACUUCUCUCUGAUGAGUCCGUGAGGACGAAACGCCCCUUUGC-3'

(SEQ ID NO:3) (Hu MT-If Rz);

5'-GAGCCUUUGCACUGAUGAGUCCGUGAGGACGAAACACAGCCCCU-3'

(SEQ ID NO:4) (Hu MT-Ib Rz);

5'-CCCCUUUGCACUGAUGAGUCCGUGAGGACGAAAUGCAGCCCCU-3'

(SEQ ID NO:5) (Hu MT-Ighlx/-II Rz);

5'-GCGCCUUUGCACUGAUGAGUCCGUGAGGACGAAACACAGCCCCU-3'

(SEQ ID NO:6) (Rz1-2); and

5'-CCUCUUUGCACUGAUGAGUCCGUGAGGACGAAAUGCAGCCCCU-3'

(SEQ ID NO:7) (Rz4-9).

28. The method of claim 27, wherein introducing the vector into the cells comprises injecting the vector directly into an *in vivo* tumor comprising the cells.

29. The method of claim 27, wherein the tumor is a human prostate tumor, a human breast tumor, or a human ovarian tumor.

30. The method of claim 27, wherein the type of therapy is radiation therapy.

31. The method of claim 30, wherein the type of radiation therapy is selected from the group consisting of external beam radiation therapy, brachytherapy, and <sup>125</sup>I administration.

32. The method of claim 27, wherein the type of therapy is chemotherapy.

33. The method of claim 32, wherein the cancer therapy agent is selected from the group consisting of cisplatin, estramustine, vinblastine, etoposide, paclitaxel, taxotere, docetaxel, doxorubicin, ketocanazole, and cyclophosphamide.

34. A ribozyme comprising a nucleotide sequence selected from the group consisting of:

5'-GCACUUCUCUCUGAUGAGUCCGUGAGGACGAAAUGCCCCUUUGC-3'  
(SEQ ID NO:1) (Hu MT-Ia Rz);

5'-CCCCUUUGCACUGAUGAGUCCGUGAGGACGAAACGCAGCCCCU-3'  
(SEQ ID NO:2) (Hu MT-Ie/r Rz);

5'-GCACUUCUCUCUGAUGAGUCCGUGAGGACGAAACGCCCCUUUGC-3'  
(SEQ ID NO:3) (Hu MT-If Rz);

5'-GAGCCUUUGCACUGAUGAGUCCGUGAGGACGAAACACAGCCCCU-3'  
(SEQ ID NO:4) (Hu MT-Ib Rz);

5'-CCCCUUUGCACUGAUGAGUCCGUGAGGACGAAAUGCAGCCCCU-3'  
(SEQ ID NO:5) (Hu MT-Ighlx/-II Rz);

5'-GCGCCUUUGCACUGAUGAGUCCGUGAGGACGAAACACAGCCCCU-3'  
(SEQ ID NO:6) (Rz1-2); and

5'-CCUCUUUGCACUGAUGAGUCCGUGAGGACGAAAUGCAGCCCCU-3'  
(SEQ ID NO:7) (Rz4-9).

35. A vector comprising a nucleic acid molecule that encodes the ribozyme of claim 34.

36. The ribozyme of claim 34, wherein the nucleotide sequence is the sequence of Hu MT-Ia Rz, Hu MT-Ie/r Rz, or Hu MT-If Rz.

37. The ribozyme of claim 34, wherein the nucleotide sequence is the sequence of Hu MT-Ib Rz or Hu MT-Ighlx/-II Rz.

38. A vector comprising two or more ribozymes, each having a nucleotide sequence selected from the group consisting of:

5'-GCACUUCUCUCUGAUGAGUCCGUGAGGACGAAAUGCCCCUUUGC-3'

(SEQ ID NO:1) (Hu MT-Ia Rz);

5'-CCCCUUUGCACUGAUGAGUCCGUGAGGACGAAACGCAGCCCCU-3'

(SEQ ID NO:2) (Hu MT-Ie/r Rz);

5'-GCACUUCUCUCUGAUGAGUCCGUGAGGACGAAACGCCCCUUUGC-3'

(SEQ ID NO:3) (Hu MT-If Rz);

5'-GAGCCUUUGCACUGAUGAGUCCGUGAGGACGAAACACAGCCCCU-3'

(SEQ ID NO:4) (Hu MT-Ib Rz);

5'-CCCCUUUGCACUGAUGAGUCCGUGAGGACGAAAUGCAGCCCCU-3'

(SEQ ID NO:5) (Hu MT-Ighlx/-II Rz);

5'-GCGCCUUUGCACUGAUGAGUCCGUGAGGACGAAACACAGCCCCU-3'

(SEQ ID NO:6) (Rz1-2); and

5'-CCUCUUUGCACUGAUGAGUCCGUGAGGACGAAAUGCAGCCCCU-3'

(SEQ ID NO:7) (Rz4-9).

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